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Research article

Application of Digital Imaging for Cytopathology under Conditions of Georgia

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Abstract: Digital imaging in cytopathology can be defined as a series of procedures, those contributing to the quality of the displayed on the computer monitor final image. The procedures include sample preparation and staining, optical image formation by the microscope and afterwards the digital image sampling by the camera sensor; which means digital image post-processing and compression, transmission across the network and display on the monitor. A large amount of data about digital imaging exist. However, there are existing the problems with standardization and understanding of the digital imaging complete process. The field of digital imaging is rapidly evolving. The new models and protocols of the digital imaging are developed around the world, but in Georgia this field is still at evolving stages and revolves around static telecytology. It has been revealed, that the application of easy available and adaptable technology together with the improvement of infrastructure conditions is the essential basis for digital imaging. This tool is very useful for implementation of second opinion consultations on difficult cases. Digital imaging significantly increases knowledge exchange and thereby ensured a better medical service. The article aims description of digital imaging application for cytopathology under conditions of Georgia.

Keywords: eHealth; digital imaging; telecytology; Internet; medical information system; second opinion consultation; cytopathology

1. Introduction

Digital imaging has undergone a period of growth and expansion catalyzed by changes in imaging hardware and gains in computational processing. Today, the digitization of entire glass slides at near the optical resolution limits of light can occur in 60s. Whole slides can be imaged in fluorescence or by use of multispectral imaging systems. Computational algorithms have been developed for cytometric analysis of cells and proteins in subcellular locations by use of multiplexed antibody staining protocols. Digital imaging is unlocking the potential to integrate primary image features into high-dimensional genomic assays by moving microscopic analysis into the digital age.

Digital imaging is highly effective and permissive application for telecytology, which is a branch of telemedicine that consists in the exchange of microscopy digital images through telecommunication with the purposes of diagnosis, consultation, research and/or education. The concept of telecytology to provide diagnostic services to remote locations was first described in the USA in 1968, when monochrome images were transmitted in real time using a dedicated point to point microwave link. In little more than a decade telecytology has developed from the prototype commercial system first described in 1986 to today's multimedia computers which can be purchased 'off the shelf' at very low prices and can be used as the basis of telecytology systems. There are technological concerns which may prevent the acceptance of telecytology by cytopathologists and thus hinder its application within the routine environment. Some cytopathologists believe that telecytology is too expensive and that it does not have a useful role in routine cytopathology. Others have doubted if computer monitors can be used for making a diagnosis, although results have shown no significant difference between a cytopathologist's performance using a microscope and using a digital image. Many of the concerns expressed about the use of telecytology are not derived from knowledge. There is a need to involve as many cytopathologists as possible in the use of these systems, particularly cytopathologists working in routine services roles. Many cytopathologists believe that fast access to expert opinion is the key to reducing the numbers of diagnostic errors, which have been estimated at up to 5%. Although most of these are not necessarily critical to the patient, some could be.

Georgia is not lagging far behind in the field of telecytology. First telecytology consultation was done in 2003. Since then a number of distance consultations were implemented. The usage of telecytology and digital imaging for quality assurance programs implementation as well as for routine cytopathology practice has been realized too. In both applications the technological platform was the medical information system. This article presents the implementation of digital images for cytopathology under the conditions of Georgia.

2. Materials and Method

2.1. Medical information system

Healthcare information technology models are constantly evolving as the industry expands. MIS is a comprehensive solution that automates the clinical, administrative and supply-chain functions. It enables healthcare providers to improve their operational effectiveness, to reduce costs and medical errors and to enhance quality of care. The aim of MIS was and is as simple as relevant: to contribute to and ensure a high-quality, efficient patient care. The relevance of 'good' MIS for high-level quality of care is obvious. Without having appropriate access to relevant data, practically no decisions on diagnostic, therapeutic or other procedures can be made.

MIS has been launched in Georgia in October, 2008. Its primary goal is patient management. However, the system is also targeted at creating a unified information space in the framework of the wider medical organization. Since first practical application of the MIS arose the idea to use it for telecytology too. Our goal was also to use MIS for telecytology purposes under the conditions of Georgia. This was a pilot study.

The MIS has been created with .Net technology and SQL database architecture. It involves a multi-user web-based approach. This ensures local (intranet) and remote (internet) access of the system and management of databases. .Net technology can be installed on computers running Microsoft Windows operating systems. It includes a large library of coded solutions to common programming problems. .Net technology is a Microsoft offering and is intended for usage by most new applications created for the Windows platform. Version 3.0 of the .Net technology included with Windows Server 2008 has been used for creation of MIS. The medical information system is object-oriented software. It is realizing client-server concept. Its architecture provides a secure, robust and extensible system for managing multiple medical terminals within a centralized depository. The MIS has a flexible architecture that can run on numerous combinations. The recommended server operating requirement is: Windows Server 2003. Hardware recommended requirements are the following: memory –1 GB, disk space –1 GB. Internet Explorer 6.0+ and/or Mozila Firefox 2.0+ can be used as client browsers. The MIS was started to create in December 2007, and the draft version was released in April 2008. After some tests and corrections, the application of ready-for-use version of the MIS started in October 2008.

2.1.1. Medical information system for cytopathology

Since March 2010 up to January 2011 100 cases in cytopathology were cared by application of medical information system. These were cases of gynecological cytology. All slides were conventional Pap smears. The slides were photographed with the 2.0 USB digital eyepiece microscope camera with resolution 3.0 MP. The images had resolution 2048 × 1536 pixels. An average number of images per case were 5 (88 cases, 88%). Each series of images per case began with a general view, followed by higher magnification of diagnostically interesting and actual areas. Cytopathologist selected these areas. The images were captured by laboratory personnel trained in the use of camera. The images were stored in a personal computer. They were adjusted by using of Adobe Photoshop. This manipulation has been done by laboratory personnel. It means the correction of image contrast and brightness. Adjusted images were uploaded to corresponding electronic medical record. All 100 electronic medical records were marked as cases for telecytology consultation. For security reasons telecytology experts have been registered as users at medical information system. Four Georgian certified cytologists were selected as experts for second opinion consultations. Cases selected for telecytology were listed at MIS home page.

For implementation of quality control mechanism each telecytology expert subjectively assessed the image quality. The ratings of image sharpness and quality were given using a 4 level scale: 1—“excellent”, 2—“good”, 3—“fair”, 4—“poor”. An average number of consultants per case were 3 (86 cases, 86%). In 94 cases (94%) the first comment was made in less than 8 hours. In 96 cases (96%) the primary diagnosis has been confirmed as a result of telecytology consultation. In 3 cases (3%) the diagnosis has been corrected. In 1 case (1%) the images were of poor quality, insufficient for remote cytology consultation.

Overall, 97.5% of the cases were rated as having excellent or good image sharpness and contrast, with 2.5% being rated as fair and poor. With respect to image color, 95% of the images were rated as excellent or good, with only 5% being rated as fair and poor. There was a high positive correlation (r = 0.83) between color, sharpness and contrast ratings. Images with excellent or good ratings generally received excellent or good color ratings. There were relatively low correlations between color (r = 0.27) and sharpness/contrast (r = 0.32) ratings and the decision confidence values.

2.1.2. Medical information system for quality assurance

For the online quality assurance program in cytopathology we randomly selected 100 gynecological cytology cases (benign: 54; atypical squamous cells of undetermined significance (ASCUS): 24; low-grade squamous intraepithelial lesion (LSIL): 7; high-grade squamous intraepithelial lesion (HSIL): 15). The randomization has been done by application of the Research Randomizer. This is a free service offered to students and researchers interested in conducting random assignment and random sampling. This service is available at www.randomizer.org. Cases were diagnosed routinely by 3 certified cytopathologists with an experience of work with digital images and usage of medical information system who provided cytology diagnoses. All participating cytopathologists have more than 7 years of cytopathology and up to 2 years' experience to work with digital images and medical information system. The most worrisome cells or groups in each cases were selected and marked by all participating cytopathologists. These areas were photographed with 2.0 USB digital eyepiece microscope camera with resolution 3.0 by cytopathologist. The images had a resolution 2048 × 1536 pixels. The mean number of selected fields and digital images for each case were 5 (range 5–7) and 20 (range 18–22), respectively. Each series of images began with a general view (magnification × 40), followed by higher magnification (× 100) of diagnostically interesting areas as directed by the cytopathologist. The images were stored in a personal computer and uploaded at medical information system (MIS) together with necessary medical data. The upload to the medical information system was done 100% successful. There was no image distortion identifiable after the upload process. Created cases were labeled "QA".

100 electronic medical records (EMRs) with cytopathology diagnosis, illustrated by images and labeled "QA" were created. Email notifications that cases are available for review have been sent to cytopathologists who already diagnosed these cases in routine manner after creation of the EMRs. These cytopathologists have been registered as users at MIS.

Diagnoses of "QA" cases were recorded in 4 categories: (1) benign; (2) ASCUS; (3) LSIL; (4) HSIL. Additional information, including comments on adequacy of images, total time required for review and problems encountered in diagnosing "QA" cases, and whether there was a need for low-magnification digital images, was recorded by each participating cytopathologist.

Diagnoses of "QA" cases correspond with initial diagnoses made in routine manner. The mean diagnostic time was 125.8 minutes (range 115–142 minutes) for glass slides and 47.3 minutes (range 38–62 minutes) for "QA" cases. Low magnification (× 40) of digital images was recorded as not necessary by all participating cytopathologists. The inability to focus at different levels to examine the architectural and cellular details of overlapping cellular groups was recorded as an impediment to diagnosis in "QA" cases.

3. Results

Perspectives and strategies for telecytology are currently evolving, as emerging operative requirements would allow self-sustainable large scale exploitation while recent technological developments are available to support integrated and cost-effective solutions to such requirements. However, as far as we know few telecytology services have proceeded to large scale exploitation, even after successful technological demonstration phases. Telecytology is the most important for the ensuring the safe medical care.

Use of telecytology consultation is appearing to have many advantages over conventional light microscopy. The International Union Against Cancer (UICC) has estimated that at least in 5–10% of cancer cases a cytopathologist need consultation during routine work because of uncertainty. Sending glass slides or paraffin blocks by mail or courier for experts in the field, is a time consuming way especially in critical specimens for cytopathologists working alone in distant hospitals with no facilities for intradepartmental consultation. Besides, the probability of loss and damage are always present. Today, telecytology in the forms of static and dynamic seems to be basic solution for this major problem. Conventional cytopathology with glass slide has many limitations. For example they may be easily broken, their stain is unstable and could fade with time, the tissue mount can bubble and dry out and finally certain procedure such as fluorescent stains are not stable more than few days. In this situation it seems that the best replacement for conventional slide cytopathology is telecytology, which never change in appearance as long as the data integrity is maintained. It is also a good approach for eLearning and already is used widely for this purpose. However, in the spite of mentioned points, telecytology in Georgia is not popular. In this article we aimed to evaluate the position of telecytology in Georgia. This is used only for consultation in limited centers and only in the form of static telecytology because of the limitations in equipment, bandwidth and high cost of internet connections, low foreign language ability and computer literacy among healthcare professionals. Another reason is the tendency of centralization of cytopathology service in Georgia. Medical information system as well as electronic medical records are not widely realized in the country. It shall be emphasized, that the most part of laboratories in Georgia are equipped by the conventional light microscopes of Soviet age. The special attention requires the quality of internet in Georgia, the internet connection in regions isn’t fast and uninterrupted. In such situation centralization of cytopathology service in Georgia means movement of patient from region to the capital for the aim to obtain the best possible care and not a transmission of the extract from the medical history illustrated by the virtual slides. It has been revealed that education and clear guidelines for cytopathologist is essential before starting telecytology. This tool is the most important thing and should be taking into account in the future planning. Because beside the benefits telecytology has no sampling error and all the things it needs are a microscope and a digital camera. We shall say that implementation of telecytology needs continuous education of cytopathologists to change their opinion about use of this tool in their routine works and taking into account the benefits of replacing conventional cytopathology by telecytology.

Healthcare IT models are constantly evolving as the industry expands. The medical information system is a comprehensive solution that automates the clinical, administrative, and supply-chain functions. It enables healthcare providers to improve their operational effectiveness, to reduce costs and medical errors, and to enhance quality of care. The aim of the medical information system was and is as simple as relevant: to contribute to and ensure a high-quality, efficient patient care. The relevance of “good” medical information system for high-level quality of care is obvious. Without having appropriate access to relevant data, practically no decisions on diagnostic, therapeutic, or other procedures can be made. In such situation, consequences will be fatal for patients. The medical information system has been launched in Georgia. The draft version was available since August 2008.

After some tests the necessary corrections and editions have been made and the working version is available since October 2008. The medical information system is used by three private medical centers located in Tbilisi, Georgia. The primary goals of this application is patient management. However, the system also targeted at creating a unified information space in the framework of the wider medical organization.

It is obvious, that digital imaging can be used in many areas of anatomic pathology, including the photography of gross and microscopic findings in both surgical and autopsy pathology. It is practical and cost-effective and provides many advantages over traditional morphology practices. Digital imaging also is the first step toward opening the door to many future applications and improved diagnostic, educational, and quality assurance activities. It is obvious, that digital imaging is rapidly becoming an integral part of the healthcare activities in many hospitals and clinics around the world. In many cases it accounts for over 50% of all eHealth activities. There are many advantages of using digital images for quality assurance in cytopathology. The major advantage is rapid turnaround time. Transmission of digital images through the internet undoubtedly is faster than the conventional method of circulating glass slides, especially when the availability of cytopathologic smears is limited compared with that of histologic material. Slow turnaround of glass slides during quality assurance exercises is a serious problem. It is reality that glass slides were circulated among more than 20 institutions throughout the country. This exercise alone took at least 3 months. Sometimes participants have to attend the meeting without viewing the slides.

The use of digital images ensures the assessment of identical fields, avoiding the problem posed by differences in field selection. The main aim in cytopathology quality assurance programs is to test participants' ability to make the correct decision on a specific abnormal finding rather than the ability to screen an entire slide. Thus, digital images circumvent the problem of field selection and assess interpretation. The time that would be spent for searching the slide for abnormal cells is eliminated. In the present study, the mean diagnostic time was reduced by more than half for "QA" cases (47.3 min) compared with glass slides (125.8 min).

It should be noted and emphasized, that the main aim in cytopathology quality assurance programs is to test participants' ability to make correct decision on a specific pathology finding. It is well known, that the specialty of cytopathology, the analysis of cellular morphology and architecture for the presence and nature of pathology, is involved in the care of virtually every patient who seeks medical attention. In a typical medical center studies have indicated that 70% of the clinical data in the electronic medical record are from cytopathology. Significantly, clinical decision support programs are highly dependent on cytopathology data. Much of the analysis performed in the cytopathology lab is visual; therefore cytopathology imaging has become an important and growing area of medical imaging environment. However, cytopathology imaging presents a number of unique challenges. Some of these challenges include the fact that cytopathology image quality is a function of many processes (many of which are outside the traditional realm of imaging). For example, image quality is a function of the processing of cellular group(s), the staining of the slide, and the ability of the microscope to form a clear, in focus image worthy of capturing. These functions and tasks are unified and standardized. Therefore the selection of the diagnostically important area is the routine procedure during screening of the entire slide and can be easily and effectively performed by the certified cytopathologist. The most important is the ability to correctly diagnose the concrete pathology finding. This ability usually correlates with a professional experience and development of this skill is the task of the cytopathology quality assurance programs.

Cost saving is another advantage. Implementation of quality assurance programs in cytopathology by usage of digital images reduces the expenses of postal or courier slide circulation and the cost and delays of photography slide preparation. Easy and continuous access to the case material from the medical information system is yet another advantage over glass slides, which have to be returned to the owner institution. After the quality assurance exercise, the digital images are still available for reference and teaching purposes. These advantages, together with the acceptable levels of diagnostic accuracy and reproducibility, strongly support the use of medical information system and digital images for cytopathology quality assurance programs.

Today, application of digital images in cytopathology seems to be basic solution for organization of quality assurance programs. Conventional cytopathology with glass slide has many limitations. For example, they may be easily broken; their stain is unstable and could fade with time, and etc. In such situation, the best replacement for conventional slide cytopathology is digital imaging. The appearance never changes as long as the data integrity is maintained. However, despite of mentioned advantages, digital imaging in Georgia is not popular. We evaluated the application of the medical information system and digital images for implementation of online cytopathology quality assurance programs under conditions of Georgia. It has been revealed that the mentioned system can be easily and effectively applied as a platform for online cytopathology quality assurance programs. The data from the present study support the use of digital images for implementation of online cytopathology quality assurance programs too. Diagnostic concordance was high (100%) for "QA" cases. The data revealed no differences between routine diagnostic versus diagnostic with digital images, supporting the reliability of using digital images displayed on a computer monitor to render accurate diagnoses and undergo online cytopathology quality assurance programs. It should be noted, however, that although there was a relatively large number of cases in this study, there were only here cytopathologists. The study would have had more power if there had been more cytopathologists.

Image quality was generally rated as excellent to good (98%). One interesting finding was that neither diagnostic decision nor diagnostic confidence was highly correlated with ratings of color, sharpness, or with viewing time. The present article illustrates that digital image include potentially eliminating the need for glass slides (at least at the point of examination), allowing annotation to be added to images, and the ability to rapidly transmit and remotely share images electronically. As it was noted above, low magnification (× 40) of digital images was recorded as not necessarily by all participating cytopathologists. The inability to focus at different levels to examine the architectural and cellular details of overlapping cellular groups was recorded as an impediment to diagnosis in "QA" cases. It has been proposed to obtain several images focusing different levels of overlapping cellular groups. This might be a solution for examination of the architectural and cellular details of such groups.

4. Discussion

Telemedicine services are rapidly becoming an integral part in many hospitals and clinics around the world. In many programs, telepathology and telecytology account for over 50% of all teleconsultations. Most studies of telepathology and telecytology have focused on usage of robotic microscopes and online microscopy. Other studies have evaluated the use of digital images of slides. Often diagnostic accuracy tends to be high, but image quality is judged to be poor. Given these equivocal results, the methods of obtaining still images as well as the adjustment of images (which usually means improvement of contrast and brightness) need to be investigated. We aimed to compare the diagnostic concordance of a cytopathology diagnoses based on routine diagnostic with a diagnoses based on digital images acquired using a digital eyepiece microscope camera and displayed on a computer monitor. We tried to evaluate the effectiveness of application of digital images for telecytology diagnostic under the conditions of Georgia too.

420 cervical smears have been reviewed and diagnosed by one of four certified cytopathologists experienced in the examination of conventional cytology smears. Each cytopathologist examines all 420 cases and rendered a single diagnosis. Diagnoses of these cases were recorded in 5 categories: (1) benign; (2) ASCUS; (3) ASC-H; (4) LSIL; (5) HSIL. After the routine cytopathology investigation the slides of all cases were photographed with the 2.0 USB digital eyepiece microscope camera with resolution 3.0 MP. The images had a resolution 2048 × 1536 pixels. Up to five images were obtained for each case. Each series of images began with a general view, followed by higher magnification of diagnostically interesting areas as directed by cytopathologist. In the actual telecytology situation, the digital images were taken by the laboratory personnel trained in the use of the digital eyepiece microscope camera. The images were transferred and stored in a personal computer. The contrast and brightness of images were adjusted by using of Adobe Photoshop. Brief patient story (age, sex, clinical diagnosis and etc.) derived from the patient's printed medical record was added into each case file. Only patient history information was included to the case. Any reference to actual diagnosis, patient name and etc. has been omitted. The 420 cases were randomized and numbered for presentation order during the study.

Approximately 100 days after all 420 cases had been diagnosed routinely, the same four cytopathologists reviewed the digital images presented on the computer. Patient history was noted prior to viewing the images for each case. A single diagnosis was rendered for each case. Subjective ratings of image sharpness and quality were given using a 4 level scale: 1—"excellent", 2—"good", 3—"fair", 4—"poor". Viewing time was recorded by a study coordinator using a stopwatch, beginning when the first image of a case appeared on the computer monitor, and ending when the cytopathologist rendered a diagnosis. The cytopathologists were restricted to 40 minutes viewing sessions. Each cytopathologist evaluated all 420 digital records, which included the images obtained from cases which routine evaluation he/she had performed. For the analysis, the routine diagnoses have been defined as the correct diagnoses. Diagnostic decisions based on digital images have been divided into two groups. Matches were those cases for which the decisions for the digital image corresponded to diagnoses rendered through routine diagnostic. If the digital image diagnosis did not match diagnose elaborated through routine diagnostic. If the digital image diagnosis did not match diagnose elaborated through routine diagnostic, the case has been classified as a mismatch (i.e., incorrect decision).

Diagnostic concordance was measured by calculating the percentage of correctly matching routine diagnoses versus digital images based diagnoses each cytologist had for all 420 cervical smears. The four cytopathologists had 94%, 93%, 92% and 97% correctly matching decisions, with 6%, 7%, 8% and 3% mismatches respectively. No statistically significant differences ($p < 0.001$) between cytopathologists in terms of percent correct decisions has been revealed. Intra-observer variation was analyzed to determine the degree to which each cytopathologist's diagnosis using the digital images agreed with their own routine diagnosis. The agreement levels were 97% ($n = 260$

cases), 99% (n =60 cases), 91% (n = 60 cases), 95% (n = 40 cases) for cytologists 1, 2, 3 and 4 respectively.

Overall, 97% of the cases were rated as having excellent or good image sharpness and contrast, with 3% being rated as fair and poor. With respect to image color, 96% of the images were rated as excellent or good, with only 4% being rated as fair and poor.

On average, it took 15.8 minutes to render a diagnosis. The minimum viewing time was 7 minutes and maximum was 22 minutes. Overall, 75% of the cases were diagnosed in less than 18 minutes. An additional 15% were diagnosed in less than 25 minutes, and 10% took longer than 30 minutes to diagnose.

5. Conclusion

We concluded that telecytology is a very useful and applicable tool for consulting on difficult cytopathology cases and can be established with very few technical equipment and software. It has significantly increased knowledge exchange, decentralization of pathology service and thereby ensured a better medical service, while simultaneously saving a lot of time and money over the previous practices.

We evaluated the application of medical information system for telepathology consultations in Georgia. It has been revealed, that mentioned system can be easily and effectively applied for remote consultations in pathology. We concluded that medical information system is a useful and applicable tool for distance consultations on difficult cases. It significantly increases knowledge exchange and thereby ensures a better medical service.

Telecytology can be conducted using a variety of technologies with varying levels of image quality and cost. The data from our studies support the use of digital images for diagnosis. Diagnostic concordance was quite high for all four cytopathologists. The data revealed no significant differences between routine diagnostic versus digital images based diagnostic, supporting the reliability of using digital images displayed on a computer monitor to render accurate diagnoses. It should be noted, however, that although there was a relatively large number of cases in this study, there were only four cytopathologists. The study would have had more power if there had been more cytopathologists.

Image quality was generally rated as excellent to good. One interesting finding was that neither diagnostic decision nor diagnostic confidence was highly correlated with ratings of color, sharpness, or with viewing time. The present data illustrates that digital image based diagnostic is a viable means for cytopathology diagnostic and can be easily applied for rural and/or regional medical centers. The advantages of digital images include potentially eliminating the need for glass slides (at least at the point of examination), allowing annotation to be added to images, and the ability to rapidly transmit and remotely share images electronically for several purposes (telecytology, conferences, education, quality assurance, peer review). In Georgia, digital images are currently utilized in telecytology, training and education (e.g. online digital atlases and eLearning cycles).

Our study revealed that digital images are a suitable substitute for online cytopathology quality assurance programs. Medical information system is a useful platform for implementation of online cytopathology quality assurance programs. But it should be also noted, that perspectives and strategies for medical information system and its practical application in routine work of the medical organization are currently evolving, as emerging operative requirements would allow self-sustainable large scale exploitation while recent technological developments are available to support integrated and cost-effective solutions to such requirements.

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Conflict of Interest

The authors claim no conflict of interest.

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